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Random Effects Analysis of Children's Blood Pressure Data

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Abstract. Some analyses of longitudinal blood pressure data have focussed on the question of whether a current value of blood pressure is predictive of subsequent rate of change. A positive correlation between blood pressure values at the beginning of a longitudinal study and rate of change over the course of the study has been found in studies of adults. Negative correlation, however, has been found in a study of children. These studies, either implicitly or explicitly, rely on linear growth curve models in which subjects' blood pressure observations are assumed to follow simple linear regression models with slopes and intercepts varying among subjects, but with the slopes constant over time.

Our analysis of a longitudinal data set of 2,203 measurements of systolic blood pressure from 216 children also provided a negative estimate of the correlation. However, smoothed plots of cross products of residuals suggested that an alternative random effects model, in which rate of change of systolic blood pressure is not treated as constant over time, might better fit the data. It is possible that the negative estimates of the correlation found in children's blood pressure data are an artifact of assuming a constant rate of change when the data actually follow the alternative model. It is shown that the expected result of fitting the linear growth curve model to data that follow the alternative model is an apparent negative correlation between slope and intercept. In the data, the observed estimates of the parameters of the linear growth curve model are consistent with the observed estimates of the parameters of the alternative model.

Key words and phrases: Autoregressive, horse-racing effect, Jenss effect, linear growth curve, Ornstein–Uhlenbeck process, random effects, regression dilution bias.

1. BACKGROUND

High blood pressure is a risk factor for stroke, heart disease and kidney failure. Affecting approximately 22% of the adult population, high blood pressure is the most common medical condition in the United States. While effective treatment is now possible for most persons with high blood pressure, relatively little is known about primary prevention.

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Although, in a few populations, average blood pressure seems to remain constant throughout life, a variety of studies have shown that the population average blood pressure generally increases with age. Some studies have examined the association between behavioral and anthropometric characteristics and blood pressure. A small but significant influence of sodium intake has been observed, and obesity and low levels of physical fitness have been found to be associated with higher blood pressure. Gender, smoking history, growth and height have also been found to be associated with higher blood pressure.

The question of whether blood pressure values tend to persist over time has been examined in longitudinal studies of blood pressure, and positive cor-

relation between baseline and subsequent measures of blood pressure values has been observed.

Investigators have also been concerned with the question of whether current values of blood pressure are predictive for subsequent rate of change. Two studies of adults, Svärdsudd and Tibblin (1980) and Wu, Ware and Feinleib (1980), have found a positive correlation between blood pressure values at the beginning of the study and subsequent rate of change. This positive correlation has been interpreted as evidence for a feedback mechanism in which high blood pressure values lead to an accelerated increase in blood pressure, and also as evidence for a so-called horse-racing phenomenon in which high blood pressure values are the eventual result of persistent positive rates of increase (Peto, 1981). In contrast to the studies showing a positive correlation between slope and intercept, one study in adults (Jenss, 1934) and one study in children (Hofman and Valkenburg, 1983) have described a negative correlation. Such negative correlations have been termed a Jenss effect.

It is generally assumed that blood pressure measurements are composed of "underlying" blood pressure values and error terms that represent measurement error and short-term transient variability. Previous investigations of correlation between initial values and subsequent slope rely, either implicitly or explicitly, on linear growth curve models in which underlying blood pressure observations are assumed to follow simple linear regression models with the slopes and intercepts varying among subjects, but with the slopes constant over time.

The presence of the error terms can lead to a kind of regression dilution bias when the naive approach of first fitting simple linear regressions to each subject's measurements and then regressing the estimated slopes on the estimated intercepts or on the initial measurements is used. See, for example, Oldham (1962). This is because the error terms induce a nonzero conditional variance, given the underlying blood pressure values, in the estimated intercept or initial measurement, and a negative conditional covariance between the estimated slope and the estimated intercept or initial measurement. If the conditional variance and correlation are not accounted for in analysis, estimates of the correlation between the slope and intercept of the underlying blood pressure are biased. In the context of longitudinal studies of blood pressure, this form of regression dilution bias has been referred to as a regression to the mean phenomenon.

Several approaches have been proposed in the context of longitudinal blood pressure data for correcting for this bias. See, for example, Blomqvist and Svärdsudd (1978), Blomqvist (1977) or Wu, Ware and Feinleib (1980). One approach is to assume Gaussian random effects and error terms, and to fit the linear growth curve model using maximum likelihood. The other is to compute sample correlations between the first observation and the estimated subject specific slopes, and then to estimate a bias correction that accounts for the conditional covariance induced by the error terms. When all of the subjects experience their first examinations at the same age, the two approaches estimate the same quantity. When subjects are not first examined at roughly the same age, it seems more natural to estimate the correlation between slope and level at a fixed age rather than to estimate a parameter that depends on the random ages at which subjects are first examined.

Differing points of view on whether the negative correlation found in adults by Jenss (1934) is wholly attributable to bias may be found in Wu, Ware and Feinleib (1980) and Hofman (1984). The negative correlation found in children by Hofman and Valkenburg (1983), however, was computed with a bias correction.

The original purpose of the analysis reported here was to examine in a longitudinal data set of children's systolic blood pressure whether there was a positive horse-racing phenomenon or a negative Jenss effect. Corresponding to the results of Hofman and Valkenburg (1983) in children, the linear growth curve analysis of the data resulted in a negative estimate of the correlation between slope and intercept. However, a graphical model-checking approach indicated that the growth curve analysis might not be appropriate. An alternative random effects model was fitted to the data. A theoretical investigation suggests that the observed results of fitting the linear growth curve analysis are consistent with the results expected when the alternative random effects model holds. It is possible that the negative covariance estimates observed with children's data are simply an artifact of applying the linear model to data that follow the alternative model.

2. DATA AND NOTATION

The data for the analysis were obtained between 1985 and 1989 as part of the longitudinal Columbia University Study of Childhood Activity and Nutrition. Subjects were healthy children recruited mainly through a pediatric practice at the Presbyterian Hospital that serves a predominately Hispanic, densely populated, low-income neighbor-

hood in northern Manhattan, New York City. Most of the children (91%) were Hispanic. Girls outnumbered boys slightly (52% to 48%). Measurements were taken at irregularly spaced intervals. See Shea, Sasch and Zybert (1989) for details of the study.

In order to maintain consistency with previous analyses, children were only included in this analysis if, after discarding the first measurement, at least six remaining longitudinal blood pressure measurements were available and the time between first and last of the remaining blood pressure measurements was at least one year. Each blood pressure measurement used in the analysis was obtained as the average of the second and third of several measurements taken at the same examination. Systolic and diastolic measurements were obtained using an automated blood pressure monitor after the child had been seated comfortably for several minutes. Only systolic blood pressure is discussed here.

There were 216 children contributing systolic blood pressure measurements to the analysis. After the first examination was excluded and after subjects with fewer than six remaining measurements were excluded, the total number of measurements included in the data was 2,203. The average of the 2,203 measurements was 100.72 mmHg, with standard deviation 8.66 mmHg and range 67.5–130.0 mmHg.

The average of the ages at the 2,203 examinations was 69.01 months with standard deviation 8.62 months and range 48.23–95.24 months. The number of examinations ranged from 6 to 13. The numbers of subjects undergoing $6, 7, \ldots, 13$ examinations were 2, 9, 18, 38, 43, 62, 42 and 2, respectively. The average number of examinations was 10.19. The average time between the first and last examination was 22.04 months.

A plot of the blood pressure measurements versus age for a set of 10 subjects is shown in Figure 1. Between-examination and between-subject variability may be seen to be of similar magnitude.

In what follows, i will index subjects and j will index examinations. The systolic blood pressure measurement obtained at the jth examination of the ith subject will be denoted by Y_{ij}. The age of the ith subject at that subject's jth measurement will be denoted by t_{ij}. The population average systolic blood pressure at age t will be denoted by $\mu(t)$.

A linear growth curve model underlies previous investigations of the association between current value and subsequent rate of change. The model posits that the difference between blood pressure and the population average may be described in terms of mean zero random intercepts and slopes plus independent error terms:

$$Y_{ij} - \mu(t_{ij}) = \alpha_i + \beta_i t_{ij} + \varepsilon_{ij}.$$

Here, α_i denotes the random intercept and β_i denotes the random slope associated with the ith subject, and ε_{ij} denotes the error term associated with the ith subject's jth measurement. The underlying blood pressure for the ith subject is $\mu(t_{ij})+\alpha_i+\beta_i t_{ij}$.

The population variance of the α_i and β_i and the population covariance between the α_i and β_i pairs will be denoted by $\sigma^2_{\alpha,\alpha}$, $\sigma^2_{\beta,\beta}$ and $\sigma^2_{\alpha,\beta}$. The variance of the ε_{ij} will be denoted by σ^2. It was assumed that the ε_{ij} are independent and independent of the α_i and β_i pairs, and for likelihood based analyses, the α_i, β_i and ε_i were assumed to have Gaussian distributions.

It will be convenient to consider reparameterizations where the intercept corresponds to blood pressure at some time τ different from zero. This model may be expressed as

$$Y_{ij} - \mu(t_{ij}) = \alpha_i^\tau + \beta_i(t_{ij} - \tau) + \varepsilon_{ij}.$$

Here α_i^τ corresponds to the ith subject's underlying blood pressure at time τ. The variance of the α_i^τ and covariance of the α_i^τ and β_i under the reparameterization are given in terms of the original parameters by

$$\sigma^2_{\alpha,\alpha}(\tau) = \sigma^2_{\alpha,\alpha} + 2\tau\sigma^2_{\alpha,\beta} + \tau^2\sigma^2_{\beta,\beta},$$
$$\sigma^2_{\alpha,\beta}(\tau) = \sigma^2_{\alpha,\beta} + \tau\sigma^2_{\beta,\beta}.$$

The parameter $\sigma^2_{\beta,\beta}$ is left invariant by the reparameterization.

It is interesting to note that the age at which the marginal variance of underlying blood pressure is minimized, $-\sigma^2_{\alpha,\beta}/\sigma^2_{\beta,\beta} = \tau - \sigma^2_{\alpha,\beta}(\tau)/\sigma^2_{\beta,\beta}$, is also the age at which the correlation between the slope and blood pressure is zero. Of course, that point might fall outside the range of the observations.

The alternative random effects model that was considered in the analysis presented here may be expressed as

$$Y_{ij} - \mu(t_{ij}) = \alpha_i + W_i(t_{ij}) + \varepsilon_{ij},$$

where α_i and ε_{ij} are as in the linear growth curve model, but where $W_i(t)$ are independent Ornstein–Uhlenbeck processes with marginal variance denoted by ω^2_W and correlation structure of the form

$$\mathrm{Corr}(W_i(t), W_i(s)) = \rho^{|t-s|}.$$

See, for example, Karlin and Taylor (1981). Rosner and Muñoz (1988) discuss this model in the context of blood pressure data. The model is considered by

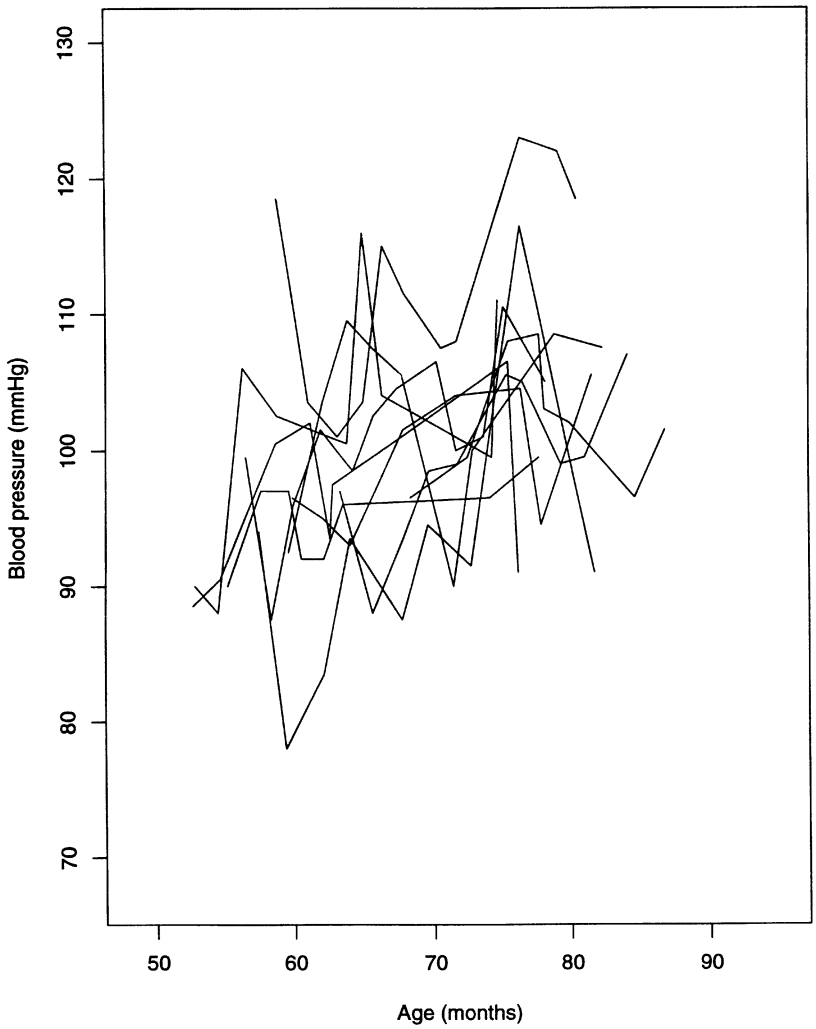

FIG. 1. *Ten representative longitudinal blood pressure profiles.*

Gillman et al. (1992) in a random effects analysis of longitudinal blood pressure data. Diggle (1988) also discusses the model. The parameter ρ is the correlation between values of W_i separated by a unit age difference. In the context of the alternative model, the variance of the α_i and ε_{ij} will be denoted by $\omega^2_{\alpha,\alpha}$ and ω^2, respectively. The α_i, the ε_{ij} and the W_i were assumed all independent. In this alternative model, the marginal variance of underlying blood pressure is constant over time and underlying blood pressure slopes vary nonlinearly over time.

3. ANALYSIS AND RESULTS

The first stage of the analysis was to estimate the population average blood pressure $\mu(t)$. Smoothed plots of the blood pressure measurements against age suggested a bent line regression, with the bend occurring at approximately 72 months of age. When the bent line regression model was estimated using ordinary least squares as if all the blood pressure measurements were independent, the estimated slope before 72 months was approximately 0.39 mmHg per month, while after 72 months it was 0.13 mmHg per month. The estimated intercept was 74.22 mmHg. A smooth and the fitted bent line regression line are pictured in Figure 2 superimposed over a plot of the blood pressure measurements against age. The smooth was computed using the `supsmu` function in the S-PLUS statistical package with the default parameters. The systematic change in the population average blood pressure is fairly small when compared with the variability in blood pressure measurements.

The next stage of the analysis was to fit the linear growth curve model. Maximum likelihood estimates of the variance components, with the intercept defined to correspond to the minimum of the ages

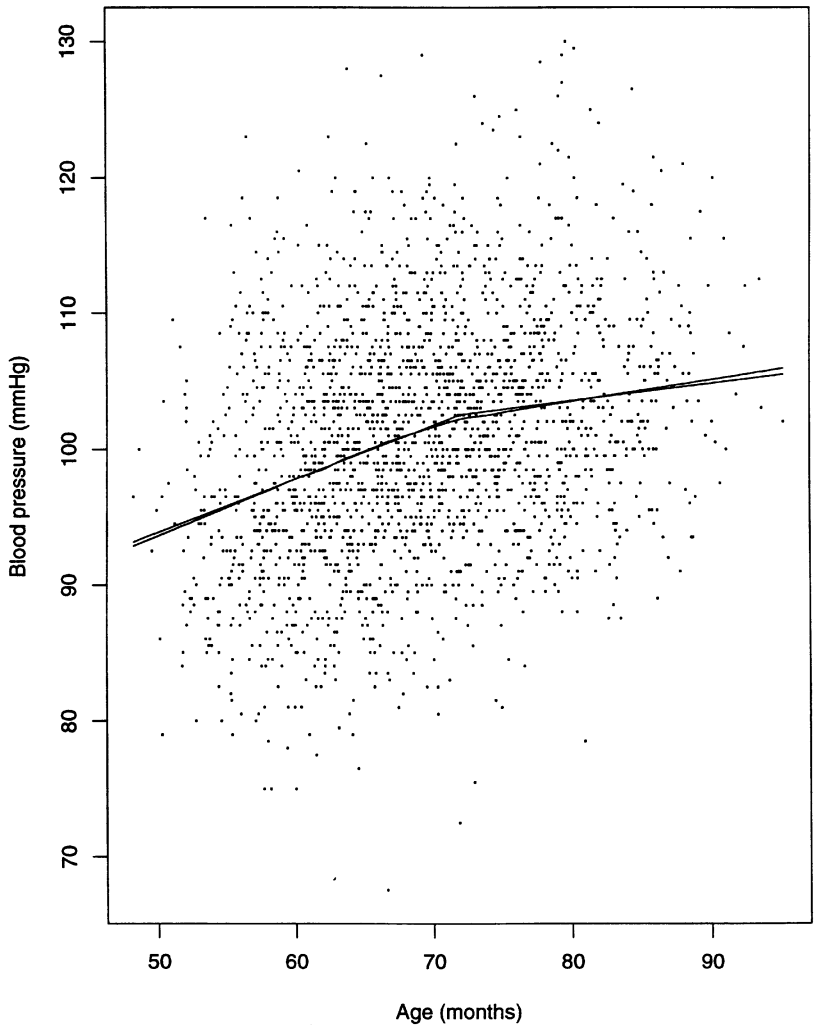

FIG. 2. *Fitted bent line regression and smooth superimposed over blood pressure measurements.*

represented in the data set ($\tau = 48$) were $\sigma^2_{\alpha,\alpha}(48) = 35.54$ mmHg^2, $\sigma^2_{\alpha,\beta}(48) = -0.34$ mmHg^2 per month, $\sigma^2_{\beta,\beta} = 0.019$ mmHg^2 per month^2 and $\sigma^2 = 38.14$ mmHg^2. Standard errors computed via the observed information matrix were 6.92, 0.22, 0.0092 and 1.28 mmHg^2, respectively. The estimate of the slope before age 72 months is 0.44 mmHg per month, and after 72 months the estimate was 0.17 mmHg per month. The estimate of the intercept (corresponding to $\tau = 48$) was 91.86 mmHg.

Note that the estimated covariance between the random intercepts (defined to correspond to the ages at the beginning of the study) and the random slopes was negative. This corresponds to the findings in children of Hofman and Valkenburg (1983). The age at which blood pressure was estimated to have minimum marginal variance was $48 - \sigma^2_{\alpha,\beta}(48)/\sigma^2_{\beta,\beta} = 66.42$ months. This was approximately the average of the ages represented in the data set.

To check the fit of the linear growth curve model, smooth plots of squares and cross-products of residuals from the fixed effect models were generated. The residuals, denoted e_{ij}, were computed as $Y_{ij} - \widehat{\mu}(t_{ij})$, where $\widehat{\mu}$ was the ordinary least squares estimate from the bent line regression model. Three plots were examined: a smooth of the scatter plot of the e^2_{ij} against the t_{ij}; a smooth contour plot of the $e_{ij_1}e_{ij_2}$ against the (t_{ij_1}, t_{ij_2}) pairs, for $j_1 \neq j_2$; and a smooth of the scatter plot of the $e_{ij_1}e_{ij_2}$ against the $|t_{ij_1} - t_{ij_2}|$, for $j_1 \neq j_2$ (Figures 3, 4 and 5). The first plot would be expected to show a quadratic function with a minimum at age $-\sigma^2_{\alpha,\beta}/\sigma^2_{\beta,\beta}$ if the linear growth curve model held, and would be expected to show a constant function if the variance were independent of age. The contour plot would be expected to show a convex quadratic with minimum at the point $(-\sigma^2_{\alpha,\beta}/\sigma^2_{\beta,\beta}, -\sigma^2_{\alpha,\beta}/\sigma^2_{\beta,\beta})$ if the linear growth curve model held. The expectation of the third plot

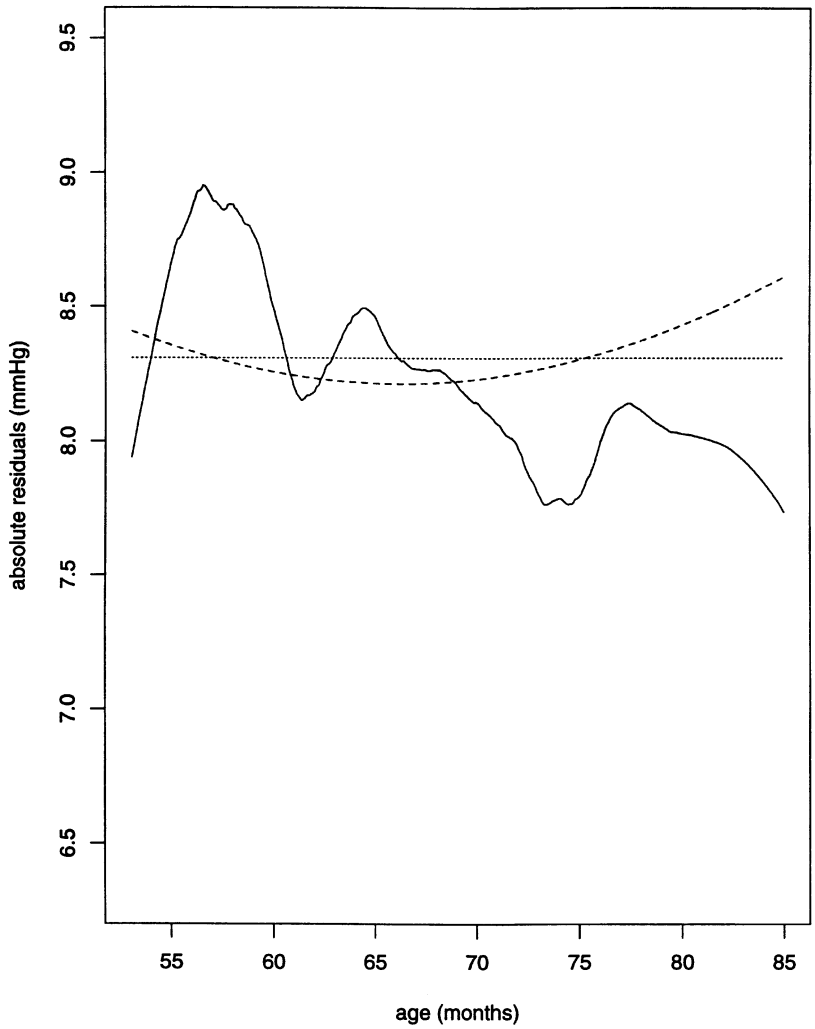

FIG. 3. *Empirical and estimated expected absolute residuals as a function of age.*

under the linear growth curve model is a complicated function of the children's ages at the examinations contributing to the data set. However, the expected smooth can be estimated by smoothing estimates of the expected cross products of residuals. The expected cross product, under the assumptions of the linear growth curve model, for observations taken at ages t_{ij_1} and t_{ij_2} is approximately

$$Ee_{ij_1}e_{ij_2} \approx \sigma^2_{\alpha,\alpha} + (t_{ij_1} + t_{ij_2})\sigma^2_{\alpha,\beta} + t_{ij_1}t_{ij_2}\sigma^2_{\beta,\beta}.$$

The first and second plots did not seem particularly useful. The problem was that the instability in the smooths, inherited from the high variability in blood pressure measurements, precluded distinguishing between the two models. In Figure 3, the square root of the smooth of the squared residuals is plotted together with the square root of the estimate of the variance expected under the fitted linear growth curve model and the alternative model. The smooth was computed using the supsmu function in the S-PLUS statistical package with the default settings. Figure 5 contains a representative version of the contour plot. The heights were computed via a kernel smooth with a kernel of the form $k(x) = \exp(-0.1\ \text{month}^{-2} \parallel x \parallel^2)$, and plotted using the contour function in S-PLUS.

The third plot, by including the large number of cross-product terms while collapsing the two-dimensional time index to the one-dimensional absolute difference, seemed to provide a fairly stable estimate. The smooth plot is shown in Figure 5 superimposed over the estimated expectation from the linear growth curve analysis and from the fit of the alternative variance components model described below. The plot suggests that the alternative model provides a superior fit.

This result may be contrasted with Gillman et al. (1992) analysis of a longitudinal data set of blood

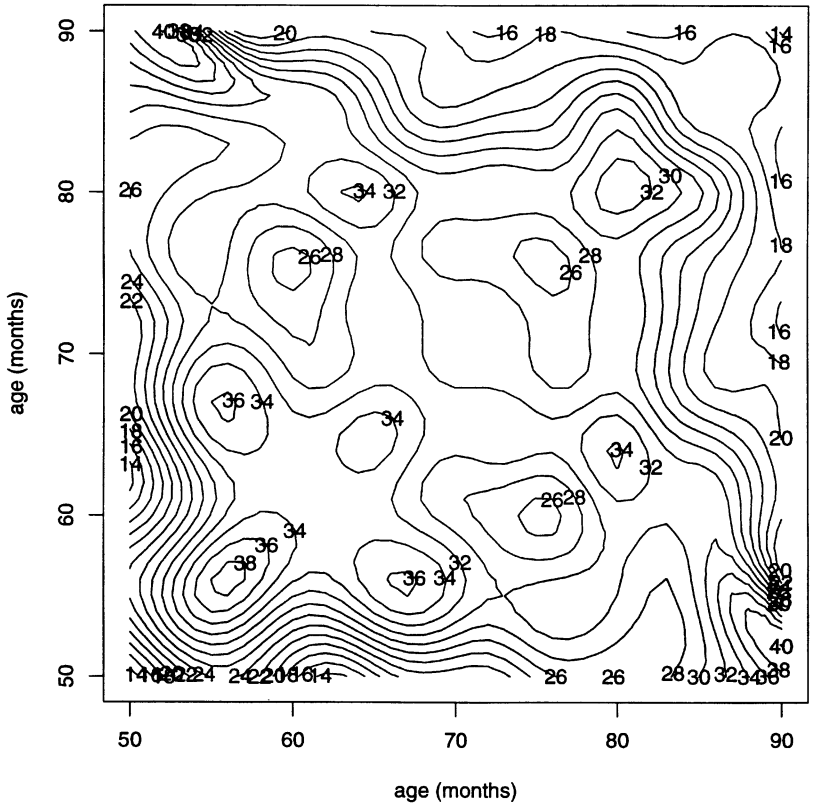

FIG. 4. *Contour plot of covariance function estimated by a kernel smooth of residual cross products.*

pressure measurements from a cohort of school children. They chose a compound symmetry model that contains neither the random slope component nor the Ornstein–Uhlenbeck component over the model with the Ornstein–Uhlenbeck process. However, the measurements in that study were performed on three annual sets of four successive weekly examinations. The correlation coefficient estimated from our data for the Ornstein–Uhlenbeck process is such that practically no information about the correlation structure of the Ornstein–Uhlenbeck component is available from measurements separated by more than six months. It is possible that even had there been a substantial component with a covariance structure close to that of the Ornstein–Uhlenbeck process, it might not have been identifiable with the sampling scheme used in Gillman et al. (1992).

The final stage of the analysis was to fit the alternative random effects model. Restricted maximum likelihood estimates of $\omega^2_{\alpha,\alpha}$, ω^2_W, ω^2 and ρ were 28.64 mmHg^2, 17.35 mmHg^2, 23.02 mmHg^2 and 0.48 month^{-1}, respectively. Standard errors were 3.26 mmHg^2, 4.79 mmHg^2, 0.10 and 4.77 mmHg^2 respectively. The estimates of the slope before age 72 months was 0.44 mmHg per month, and the estimate of the slope after age 72 months was 0.20 mmHg per month. The estimate of the intercept was 70.77 mmHg. The standard error for the difference in slopes was 0.06 mmHg per month. Note that the Ornstein–Uhlenbeck component was estimated to account for a substantial portion $(17/(28 + 17 + 23) \approx 25\%)$ of the variability of blood pressure. The estimate of ρ corresponds to negligible correlation in the Ornstein–Uhlenbeck process after approximately five or six months $(\rho^5 = 0.03,\ \rho^6 = 0.01)$.

All of the maximum likelihood and restricted maximum likelihood analyses were based on assuming Gaussian distributions for the random effects and error terms. See, for example, Laird and Ware (1982) or Harville (1977). Computations were carried out using the SAS statistical package routines PROC GLM and PROC MIXED.

4. FITTING THE LINEAR MODEL TO NONLINEAR DATA

In this section, the expected behavior of fitting the linear growth curve model to data that follow the alternative model is explored. For the sake of simplicity, attention is restricted to the special case

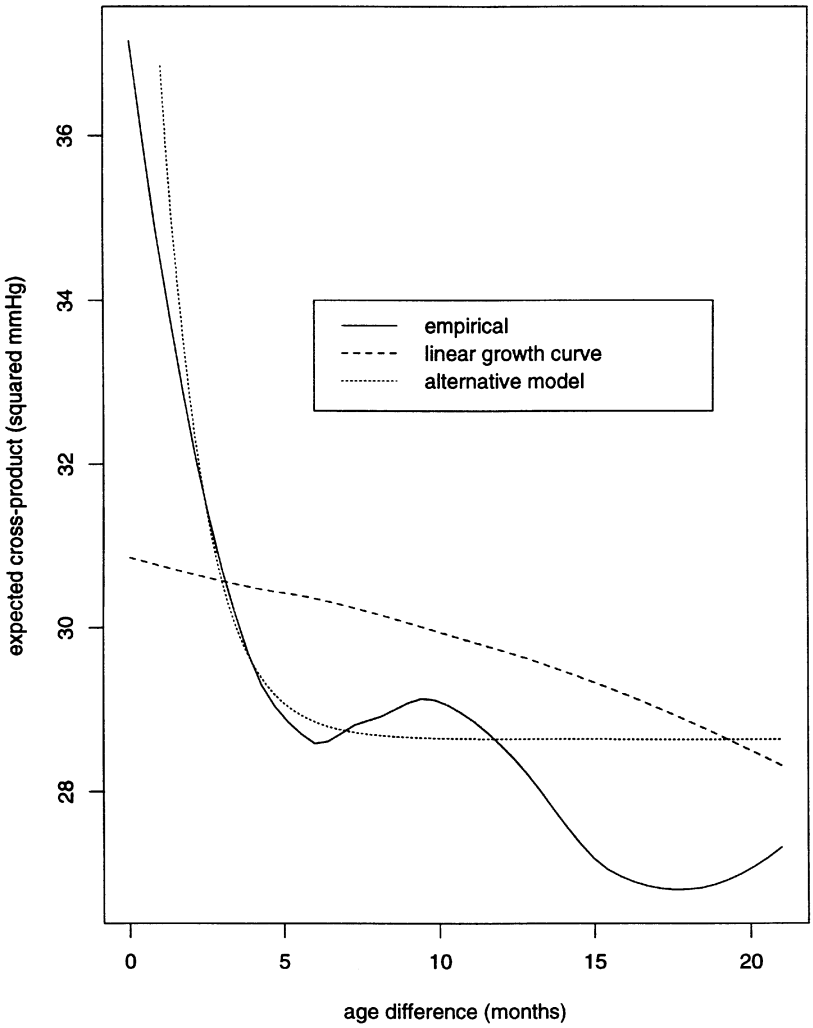

FIG. 5. *Expected residual cross products as a function of absolute age difference.*

in which the subjects are all examined at the same ages, μ is assumed to be zero and the examination ages are symmetric around the average age.

Let $t_1, t_2, \ldots, t_k$ denote the sequence of examination ages and let $\bar{t}$ denote their average. Let $\bar{Y}_i$ denote the average of the Y_{ij}, let $\widehat{\beta}_i$ denote the ith subject's estimated slope,

$$\widehat{\beta}_i = \sum_{i=1}^{k} (Y_{ij} - \bar{Y}_i)(t_i - \bar{t})/T,$$

where

$$T = \sum_{j=1}^{k} (t_j - \bar{t})^2.$$

Let s_i^2 denote the sum of squared residuals,

$$s_i^2 = \sum_{j=1}^{k} (Y_{ij} - \bar{Y}_i - (t_j - \bar{t})\widehat{\beta}_i)^2,$$

In the linear growth curve model, the s_i^2, $\bar{Y}_i$ and $\widehat{\beta}_i$ are sufficient with the s_i^2 distributed as $\sigma^2 \chi^2_{k-2}$ independent of the $(\bar{Y}_i, \beta_i)$ pairs and the covariance of the pairs is given by

$$\begin{pmatrix} \sigma^2_{\alpha,\alpha} + \sigma^2/k & \sigma^2_{\alpha,\beta} \\ \sigma^2_{\alpha,\beta} & \sigma^2_{\beta,\beta} + \sigma^2/T \end{pmatrix}$$

so that the zeros of the expected score equations satisfy

$$\sigma^2 = \frac{E s_i^2}{(k-2)},$$

$$\sigma^2_{\alpha,\alpha}(\bar{t}) + \sigma^2/k = E\bar{Y}_i^2,$$

$$\sigma^2_{\beta,\beta} + \frac{\sigma^2}{\sum_{j=1}^{k}(t_j - \bar{t})^2} = E\widehat{\beta}_i^2,$$

$$\sigma^2_{\alpha,\beta}(\bar{t}) = E\bar{Y}_i\widehat{\beta}_i.$$

Evaluating the expectations under the assumptions of the alternative model, and solving reveals that the solutions to the expected score equations

are

$$\sigma^2 = \omega^2 + \frac{\omega_W^2}{k-2}\left(k - \sum_{j_1=1}^{k}\sum_{j_2=1}^{k}\rho^{|t_{j_1}-t_{j_2}|} \cdot \left(\frac{1}{k} - \frac{(t_{j_1}-\bar{t})(t_{j_2}-\bar{t})}{T}\right)\right),$$

$$\sigma^2_{\alpha,\alpha}(\bar{t}) = \omega^2_{\alpha,\alpha} - \frac{1}{k}\frac{\omega_W^2}{k-2}\left(k - \sum_{j_1=1}^{k}\sum_{j_2=1}^{k}\rho^{|t_{j_1}-t_{j_2}|} \cdot \left(\frac{1}{k} - \frac{(t_{j_1}-\bar{t})(t_{j_2}-\bar{t})}{T}\right)\right),$$

$$\sigma^2_{\alpha,\beta}(\bar{t}) = \sum_{j_1=1}^{k}\sum_{j_2=1}^{k}\omega_W^2\rho^{|t_{j_1}-t_{j_2}|}\frac{t_i-\bar{t}}{kT},$$

$$\sigma^2_{\beta,\beta} = \omega_W^2\sum_{j_1=1}^{k}\sum_{j_2=1}^{k}\rho^{|t_{j_1}-t_{j_2}|}\frac{(t_{j_1}-\bar{t})(t_{j_2}-\bar{t})}{T^2} - \frac{1}{T}\frac{\omega_W^2}{k-2}\left(k - \sum_{j_1=1}^{k}\sum_{j_2=1}^{k}\rho^{|t_{j_1}-t_{j_2}|} \cdot \left(\frac{1}{k} - \frac{(t_{j_1}-\bar{t})(t_{j_2}-\bar{t})}{T}\right)\right).$$

It may be calculated that for symmetric values of the examination times, the solution corresponding to $\sigma_{\alpha,\beta}(\bar{t}) = 0$, while the solution corresponding to $\sigma_{\beta,\beta}$ is positive. It follows that the estimate of the correlation between underlying blood pressure value at the first examination time and the slope of the underlying blood pressure will be negative.

These formulae may be evaluated at the values of the estimated parameters of the alternative model. The average number of examinations in the data set was between 10 and 11, and the average time between the first and last examinations was approximately 22 months. When the formula for the expectation of the estimate of $\sigma^2_{\beta,\beta}$ evaluated with 11 equally spaced examinations ranging over 22 months, and with the variance components of the alternative model given by those estimated from the data, the result is 0.013. This is not far from the estimated value, 0.019. The corresponding expected estimates of $\sigma^2_{\alpha,\alpha}(\bar{t})$ and σ^2 are 27.2 and 38.89. The corresponding maximum likelihood estimates of $\sigma^2_{\alpha,\alpha}(69)$ and σ^2 were 29.22 and 38.14. The estimates obtained from the linear growth curve model are quite close to those that are predicted using the estimated parameters of the alternative model.

5. DISCUSSION

The original purpose of this investigation was to determine whether there was a horse-racing phenomenon or a Jenss effect in a longitudinal data set of children's systolic blood pressure. An initial analysis based on a model in which each subject's underlying blood pressure differed linearly over time from the population average suggested a Jenss effect: fitting the linear growth curve model resulted in a negative estimate of the correlation between the underlying systolic blood pressure value at the beginning of the study and the slope of the underlying blood pressure. The age at which underlying blood pressure is independent of slope was estimated to be at approximately the midpoint of the study.

The linear growth curve model is suspect, however, both on a priori and empirical grounds. The linearity constraint implies the unnatural situation that an underlying blood pressure trajectory that begins on a given course must maintain that course without deviation. Underlying blood pressure values that move away from a given level are constrained by the definition of the model never to return to that level. In addition, the graphical model checking approach suggested that an alternative random effects model fits our data better than the linear growth curve model.

Interpretation of the apparent Jenss phenomenon presents a paradox. The result of the linear growth curve analysis suggests that this difference between an individual's underlying blood pressure and the population average blood pressure begins either above or below a subject-specific level, crosses that level at approximately the midpoint of the study and then continues along the same trajectory to end up on the opposite side of the level. A possible resolution of the paradox may be found in the theoretical investigations that indicate that the apparent Jenss phenomenon can be explained as an artifact of fitting the linear growth curve model to data that follow the alternative model. An intuitive explanation of the theoretical result may be found in recognizing that as long as the magnitude of the Ornstein–Uhlenbeck component is large enough to cause a significant positive estimate of the variance of the random slope term, the stationarity of the alternative model will place the estimate of the age at which level and slope are independent at approximately the midpoint of the study. Accordingly, a typical trajectory with a negative slope will start the study at relatively higher value and a typical trajectory with a positive slope will start the study at a relatively lower value.

Some caution should be used in extrapolating this explanation of the apparent Jenss phenomenon to other studies. Gillman et al. (1992) did not find the Ornstein–Uhlenbeck component in their data. However, their sampling plan, while quite effective in differentiating between long term, fairly short

term and completely transient components of variance was probably not very sensitive to the moderately persistent Ornstein–Uhlenbeck component estimated in our data.

As it is known that a variety of transient behavioral and environmental factors influence blood pressure, it is not surprising to find a nonlinear component of variance in children's blood pressure. It would be of interest to collect blood pressure data at a high sampling density and in tandem with accurate measures of factors that influence blood pressure to explore which factors are responsible for long term differences in underlying blood pressure and which are responsible for transient changes.

Finally, it might be noted that, although Figure 5 suggests the Ornstein–Uhlenbeck structure and the theoretical calculations show that the result of fitting the linear growth curve model are consistent with an Ornstein–Uhlenbeck component, the Ornstein–Uhlenbeck component is at best only an approximation to the effect of the transient factors that influence blood pressure. A nongraphical approach to comparing the fit of the Ornstein–Uhlenbeck model and the linear growth curve model would be to fit a model that included both kinds of components. The likelihood for models that fit both kinds of components, however, is not very well behaved. The Newton–Raphson approach to maximizing the likelihood is very sensitive to the choice of starting points. With some starting points, the algorithm fails to converge, and with others it converges at untenable parameter values. If starting points are chosen to correspond to a model with only the Ornstein–Uhlenbeck component, then the algorithm iterates to a solution with a negligible linear growth curve component. On the other hand, if starting points are chosen to correspond to a model with only the linear growth curve component, then the algorithm iterates to a solution with no Ornstein–Uhlenbeck component. The estimated parameters resulting from starting at a model with no linear growth curve component are $\sigma^2_{\alpha,\alpha} = 28.59$ mmHg^2, $\sigma^2_{\alpha,\beta} = 0.10$ mmHg^2 per month, $\sigma^2_{\beta,\beta} = 0.0012$ mmHg^2 per month^2, $\sigma^2_W = 17.49$ mmHg, $\rho = 0.48$ month^{-1} and $\sigma^2_\varepsilon = 22.73$ mmHg^2. The p-values for testing whether $\sigma_{\beta,\beta}$ and $\sigma_{\alpha,\beta}$ are zero were 0.90 and 0.36, respectively, and the p-value for the composite hypothesis that both parameters are zero was 0.65. The fitted log likelihood for the model with slopes and intercepts only was -7483; for the model with the Ornstein–Uhlenbeck component only, it was -7939; and for the model with both but with starting points corresponding to the Ornstein–Uhlenbeck component only, it was -7397.

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